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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,134	10/20/2002	Chandrasekhar Satishchandran	NUCL-001/01US 311248-2006	5538
90162	7590	11/18/2009	EXAMINER	
David S. Resnick Nixon Peabody LLP 100 Summer Street Boston, MA 02110			CHONG, KIMBERLY	
			ART UNIT	PAPER NUMBER
			1635	
			MAIL DATE	DELIVERY MODE
			11/18/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/009,134	SATISHCHANDRAN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 107-114, 116-136, 138-140, 142-145, 147, 157-167 and 172-174 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 107-114, 116-136, 138-140, 142-145, 147, 157-167 and 172-174 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>07/09/2009</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Status of Application/Amendment/Claims***

Applicant's response filed 08/20/2009 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 05/20/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 08/20/2009, claims 107-114, 116-136, 138-140, 142-145, 147, 157-167 and 172-174 are pending and currently under examination in the application.

### ***Re: Double Patenting***

Acknowledgement is made of Applicant's request that the rejection be held in abeyance until allowable matter is indicted in the instant claims, therefore the rejection of claims 107-114, 116-136, 138-140, 142-145, 147, 157-167 and 172-174 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 119-135 of copending Application No. 10/836,856 is maintained.

### ***Re: Claim Rejections - 35 USC § 112 - withdrawn***

The rejection of claims 107-114, 116-136, 138-140, 142-145, 147, 157-167 and 172-174 under 35 U.S.C. 112, first paragraph, is withdrawn in response to claim amendments.

The rejection of claims 139 and 174 under 35 U.S.C. 112, first paragraph, is withdrawn in response to claim amendments.

***Re: Claim Rejections - 35 USC § 103 - maintained***

The rejection of claims 107-114, 116-136, 138-140, 142-145, 147, 157-167 and 172-174 under 35 U.S.C. 103(a) as being unpatentable over Werther et al. (cited on PTO Form 892 filed 08/07/2006), Fire et al. (cited on PTO Form 892 filed 08/07/2006), Heifetz et al (cited on PTO Form 892 filed 08/07/2006), Calabretta et al. (US Patent No. 5,734,039 cited on PTO Form 892 filed 03/08/2007), Taira et al. (cited on PTO Form 892 filed 11/22/2005) and Thompson et al. (cited on PTO Form 892 filed 08/07/2006) is maintained for the reasons of record.

The rejection of claims 107-114, 116-136, 138-140, 142-145, 147, 157-167 and 172-174 under 35 U.S.C. 103(a) as being unpatentable over Taira et al. (cited on PTO Form 892 filed 11/22/2005), Fire et al. (US Patent No. 6,506,559 of record 892 filed 08/07/2005) and Thompson et al. (cited on PTO Form 892 filed 08/07/2006) is maintained for the reasons of record.

Applicant's arguments filed 08/20/2009 have been fully considered but they are not persuasive. Applicant argues there is no motivation to combine the references because the methods of expression inhibition in the cited references are not interchangeable. Applicant states that it is clear from the description that the double

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stranded regions of the RNA sequences interact with the target gene in contrast to the mechanisms involved in both ribozyme and antisense mediated inhibition where the single stranded regions of said molecules permit target recognition. In addition, Applicants argue that the skilled artisan would recognize the claimed invention is directed to an siRNA-like mechanisms which is different that the cited art referencing both ribozymes and antisense molecules. Because of these differences, Applicant argues the skilled artisan would not be motivated to use the methods of Taira et al. and Thompson et al. drawn to ribozymes or Werther et al. and Calabretta et al. drawn to antisense molecules.

Applicant's arguments are not convincing because the rejection of record is not based on substituting the methods of ribozymes or antisense molecules for the claimed multitarget partially double stranded RNA molecule.

Heifetz et al. does in fact teach expression vectors comprising two or more different double stranded RNA sequence wherein the dsRNA sequences are complementary to target sequences and capable of mediating inhibition of target gene expression. Heifetz et al. do not teach the sequences are complementary to two or more sequences of at least one mammalian target gene and therefore Werther et al. and Calabretta et al. were cited because they both teach the advantages of targeting two or more sequences of at least one target gene because certain target sequences are capable of mutation and targeting multiple sites on a target gene is advantageous for making effective therapeutics. There is nothing in the rejection of record that requires the use of the methods of the cited references. Moreover, it is well known in the

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art that ribozymes, antisense molecules and siRNA all cleave the target RNA by different mechanisms however it is also well known in the art that each of the molecules require a single stranded antisense sequence that recognizes and binds to the target RNA to mediate cleavage of the target RNA and inhibition of expression which is the common purpose of each of the molecules. Thus, one of ordinary skill in the art would have found the approach to simultaneous targeting of genes taught by Werther et al. and Calabretta et al. applicable to the claimed RNA molecule.

In response to Applicant's arguments regarding Taira et al. and Thompson et al., Heifetz et al., while teaching vectors comprising two or more different double stranded RNA sequence wherein the dsRNA sequences are complementary to target sequences and capable of mediating inhibition of target gene expression do not teach said expression vector expresses two different double stranded RNA sequences using two promoters wherein the promoters are RNA pol III promoters. Taira et al. demonstrates that it was well known in the art to use expression vectors comprising cleavage sequences for expressing multiple RNA molecules that are capable of mediating inhibition of target gene expression. Further, Thompson et al. demonstrates it was well known in the art to incorporate a RNA pol III promoter into the expression vector because said promoters are more attractive for expression of RNAs in all tissue types and the accumulation in the cells is greater from a pol III based expression vector. Thus, one of ordinary skill in the art would have found the expression vectors taught by Taira et al. and the use of RNA pol III promoters taught by Thompson et al. applicable to

the claimed invention and would have had a reasonable expectation of success at generating an expression vector comprising one or more different RNA molecules.

Therefore, it would have been obvious to one of skill in the art to make a multitargeted double stranded RNA wherein said double stranded RNA targets at least one or more than one target gene given the advantages taught by Werther et al. and Calabretta et al. and further it would have been obvious to use expression vectors comprising two promoters for expressing said dsRNAs as taught by Taira et al. and Thompson et al.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-

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3111. The examiner can normally be reached Monday thru Thursday between 6 and 3 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Tracy Vivlemore at 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/  
Primary Examiner  
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